

REMARKS/ARGUMENTS

I. The Outstanding Rejections.

Claims 7-10 stand rejected under 35 U.S.C. §112 (second paragraph) as indefinite.

Claims 7-10 stand rejected under 35 U.S.C. §103(a) Over Godiska, U.S. 5,759,804 in view of Shen EP 0 726 310.

II. Preliminary Remarks

The present invention relates to the discovery (1) that there is a self-annealing problem with dried primers and (2) that the solution to that problem is the use of shorter dried primers. Accordingly, the invention provides methods of forming random mixtures of oligonucleotides which are resistant to self-annealing and relates to the recognition that the self-annealing problem is specific to 9-mers (and longer oligonucleotides) used in dried kits and does not represent such a problem with shorter dried primers.

In reaching its decision on appeal the Board of Patent Appeals and Interferences declined to reach the merits of the rejection under 35 U.S.C. §112 (first paragraph) because it affirmed the rejection of claims 7-14 under 35 U.S.C. §103.

III. The Rejections Under 35 U.S.C. § 112 (second paragraph) Should be Withdrawn.

The indefiniteness rejection of claims 7-10 under 35 U.S.C. § 112, second paragraph, should be withdrawn because the two steps of “selecting a random mixture of oligonucleotides” and “drying the mixture” would be readily understood by a worker of ordinary skill in the art to achieve the goals of the claimed invention.

The Examiner contends that it is unclear what is meant by “selecting” a random mixture of oligonucleotides, and suggests that a worker of skill in the art could not select a mixture of random primers having self-annealing-resistant properties. The first step of “selecting a random mixture of oligonucleotides” is readily understood by those of ordinary skill in the art of DNA synthesis as simply choosing or using a random collection of oligonucleotides of a specific nucleotide length. For example, Godiska, at col. 8, lines 26-31, describes preparing a DNA probe using a denatured DNA fragment, dNTP's, “random hexamer primers” and DNA polymerase. Hoeltke et al., (US 5,814,502, cited in Office

Action of 8/8/03) describe a DNA priming reaction using a specified amount of “random primer” (col. 4, lines 15-30). A worker of ordinary skill readily appreciates that generating or obtaining random nucleotides of a specific length is the “selecting” that is performed.

To the extent that the Examiner implies that the unexpected results obtained by practice of the invention result from a selection of primers having particular sequences, this is not the case. In fact, such a selection would, by definition, not be random. Applicant’s primers are random, meaning they comprise essentially all sequences for a given length. The unexpected properties result because they are short (6-8 mers) and dried.

The Examiner’s rejection on the basis that it is unclear after which step the end result of the claim is achieved should be withdrawn because the second and final process step of the claims is clearly stated to be “drying said mixture.” The steps of selecting a random mixture of oligonucleotides and then drying the mixture complete the method of forming self-annealing resistant primers. Applicant’s invention is clearly directed to “a method of forming a random mixture of oligonucleotides which is resistant to self-annealing.” It is just as clear that the method comprises two steps, a) selecting a random mixture of oligonucleotides which are 6 mers to 8 mers; and b) drying that mixture.

Because no evidence or rationale had been presented that one of ordinary skill would not appreciate what is and what is not covered by the claims the rejection under §112, second paragraph, should be withdrawn.

IV. The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn.

The application Examples demonstrate a critical and unexpected difference in self-priming activity and labeling intensity between 6-8 mers and 9-mers and there is no teaching in the art that such a difference could occur. Accordingly, the obviousness rejection under 35 U.S.C. §103(a) should be withdrawn because the art fails to teach the desirability of short primers (6-8 mers) in a dried primer system or that 6-mers to 8-mers would behave differently with respect to self-priming activity and labeling intensity than do 9-mers.

More specifically, Godiska discloses liquid 6-mers but fails to teach (1) that the selection of 6-mers to 8-mers constitutes a critical range or (2) that short primers (6-8 mers) would be desirable in a dried primer system. While Godiska discloses a random mixture of

6-mers and other ingredients the Examiner acknowledges that Godiska does not teach a labeling composition in a dry state. Moreover, there is nothing in Godiska that teaches that the selection of 6-mers to 8-mers is important in either the liquid or freeze dried state to reduce self-annealing. In fact, self annealing is not mentioned at all!

In addition, Shen discloses 48-mer and 22-mer primers and fails to suggest that dried primers should be shortened or alternatively any reason why the primers of Godiska should be dried. This is because the prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures and are thus more specific.

Moreover, Shen acknowledges that "whether a particular composition will function to preserve biological activity for a particular biologically active material is not a priori predictable" (page 4, lines 36-37) and only discloses freeze-drying as an "option" (pg 5, lines 14-15) and In addition, Shen fails to provide any reason why the primers of Godiska should be dried given the fact that shorter primers were thought to be inherently more stable and there was no reason to believe that the shorter Godiska primers would benefit from being in freeze-dried kits.

The Board rejected these arguments on the basis that applicants showing of unexpected results was insufficient to rebut a prima facie case of obviousness because "the closest prior art [to dried 6-mer primers] is not dried nonamers, but random 6-mer primers that have not been dried, as taught by Godiska." This argument is incorrect because the closest prior art to dried 6-mers is dried 9-mers! Because the rejection is an obviousness rejection the closest prior art is the prior art that those of ordinary skill in the art would consider most relevant and would have been most motivated to practice. For the reasons set out above, the bias in the art was toward longer rather than shorter primers at the same time it taught dried primers rather than primers in solution. Thus, the person of ordinary skill in the art would have been motivated to modify the short wet primers of Godiska to the long dry primers of Shen, not to the short dried primers of the invention. Because the claimed invention is unobvious over what was taught by the prior art and preferred by those of skill in the art at the time of Applicant's invention it is neither necessary nor appropriate to make comparisons over different compositions that were not preferred by the art.

For these reasons, the rejections under 35 U.S.C. §103 (a) should properly be withdrawn. Should the Examiner have any questions or comments of form or substance, she is encouraged to contact the undersigned attorney.

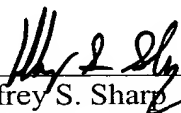
CONCLUSION

In view of the foregoing remarks, claims 7-10 are believed to be in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested. Should the Examiner have any concerns of either form or substance she is encouraged to contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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